=> dis his

(FILE 'HOME' ENTERED AT 12:33:59 ON 23 SEP 2003)

FILE 'REGISTRY' ENTERED AT 12:34:08 ON 23 SEP 2003

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L3         3163 S L1 FUL
L4              STR
L5            0 SEARCH L4  SUB=L3 FUL
L6              STR L4
L7            0 SEARCH L6  SUB=L3 FUL
L8              STR L6
L9            0 SEARCH L8  SUB=L3 FUL
L10             STR L8
L11           0 SEARCH L10  SUB=L3 FUL
L12             STR L1
L13             STR L12
L14          50 S L13
L15        3163 SEARCH L14  SUB=L3 FUL
L16             STR L13
L17        3151 SEARCH L16  SUB=L15 FUL
L18             STR L1
L19        2812 SEARCH L18  SUB=L17 FUL
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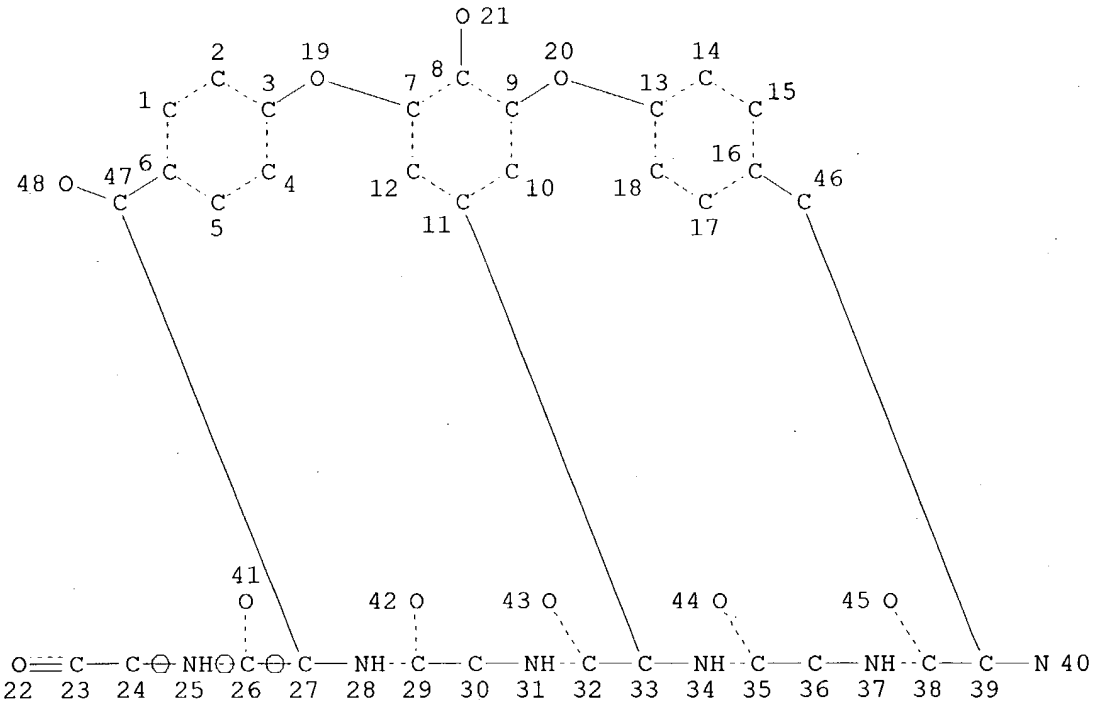
Str (I) Compound pg 67 extremely broad.

=> d l11 que stat;d l19 que stat;fil medl,caplus,biosis,embase;s l19 and (linsell, m? or judice, j?)/au

L1 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

Searched by: Mary Hale 308-4258 CM-1 1E01

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 48

STEREO ATTRIBUTES: NONE
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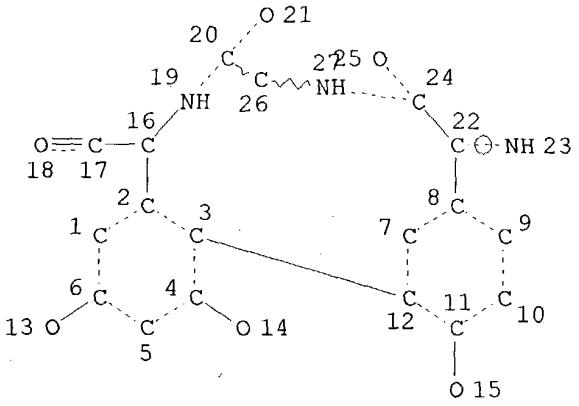
L10 STR



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STEREO ATTRIBUTES: NONE
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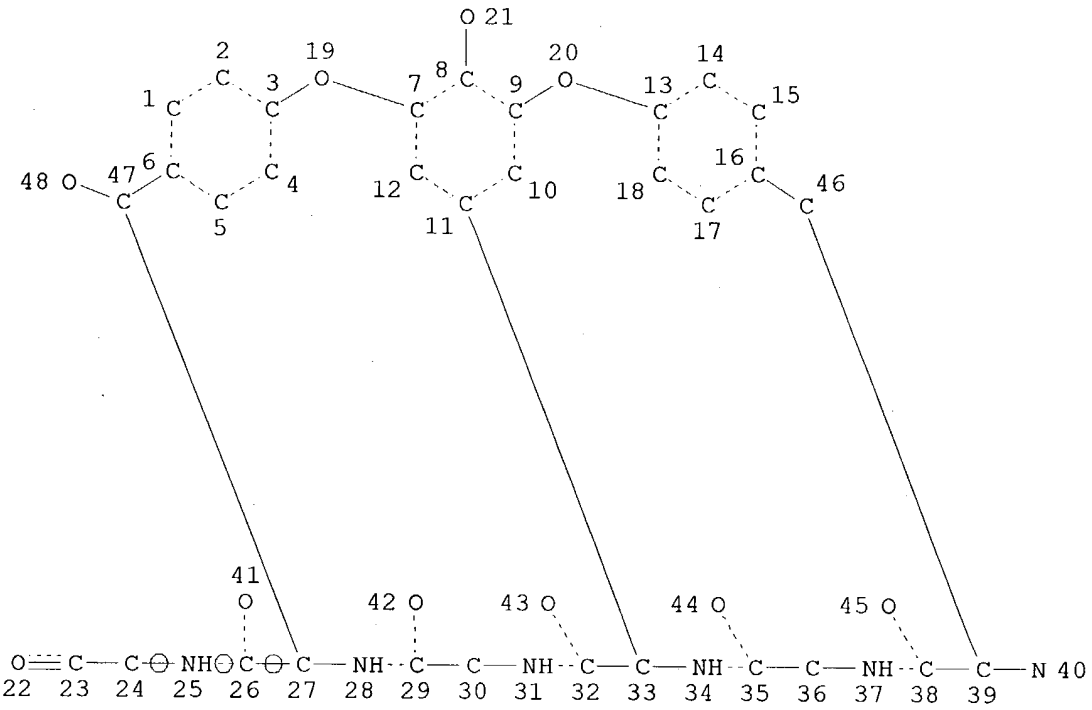
SEARCH TIME: 00.00.01

L1 STR

Searched by: Mary Hale 308-4258 CM-1 1E01



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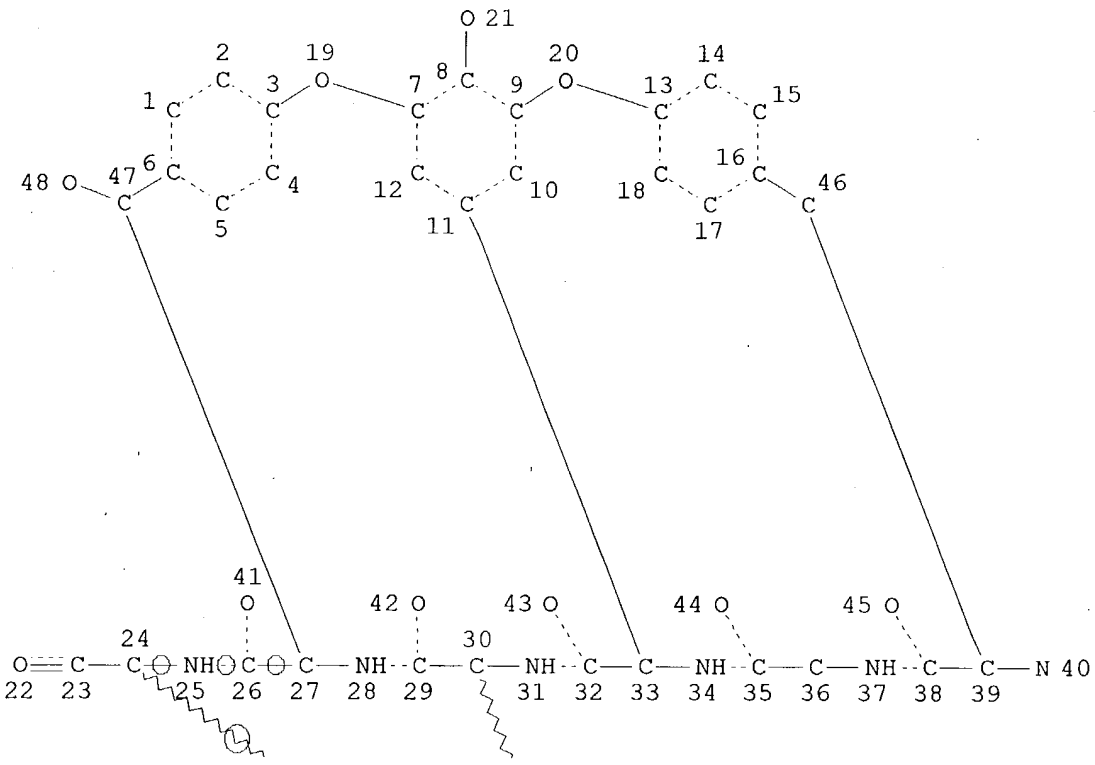
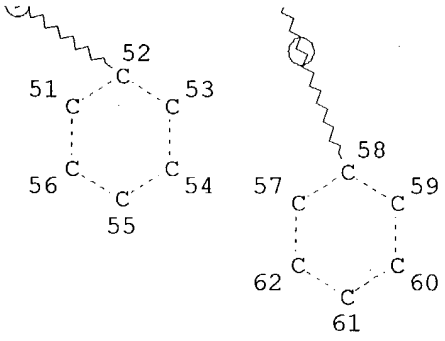
Searched by: Mary Hale 308-4258 CM-1 1E01



Page 1-A



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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 60

STEREO ATTRIBUTES: NONE
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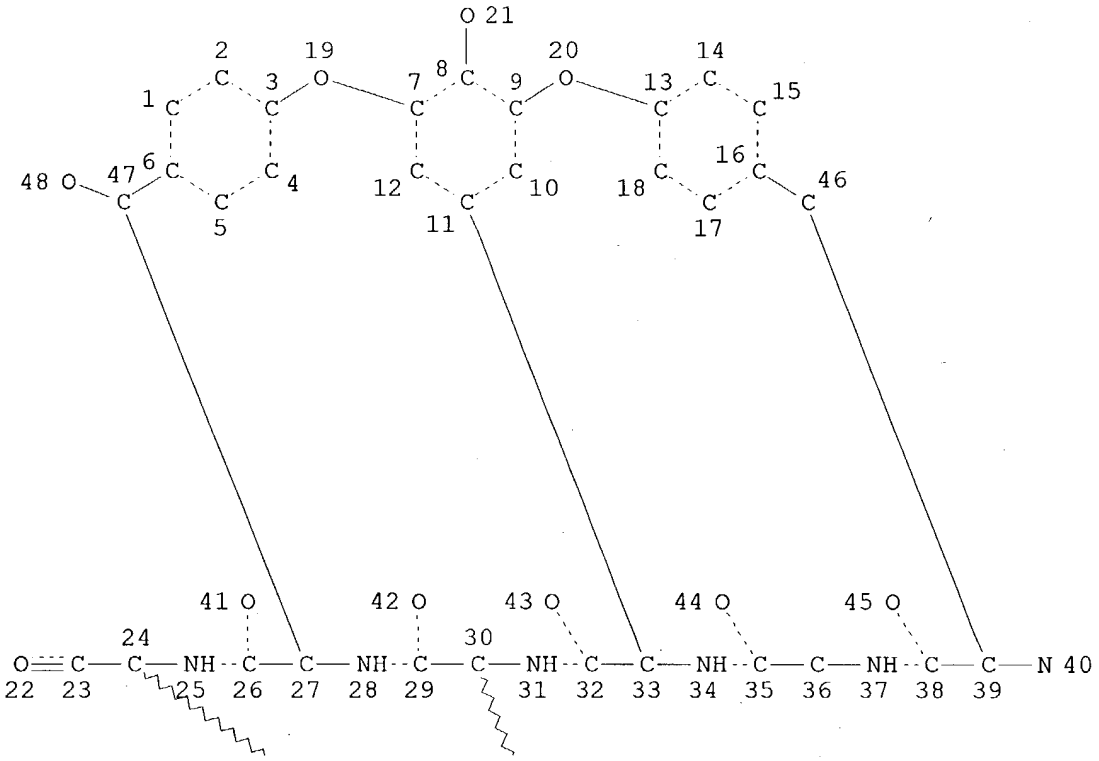
Searched by: Mary Hale 308-4258 CM-1 1E01



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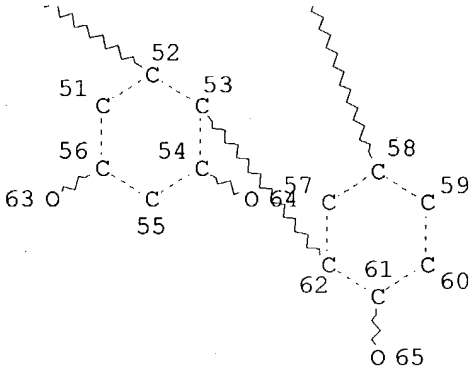

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GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 63

STEREO ATTRIBUTES: NONE
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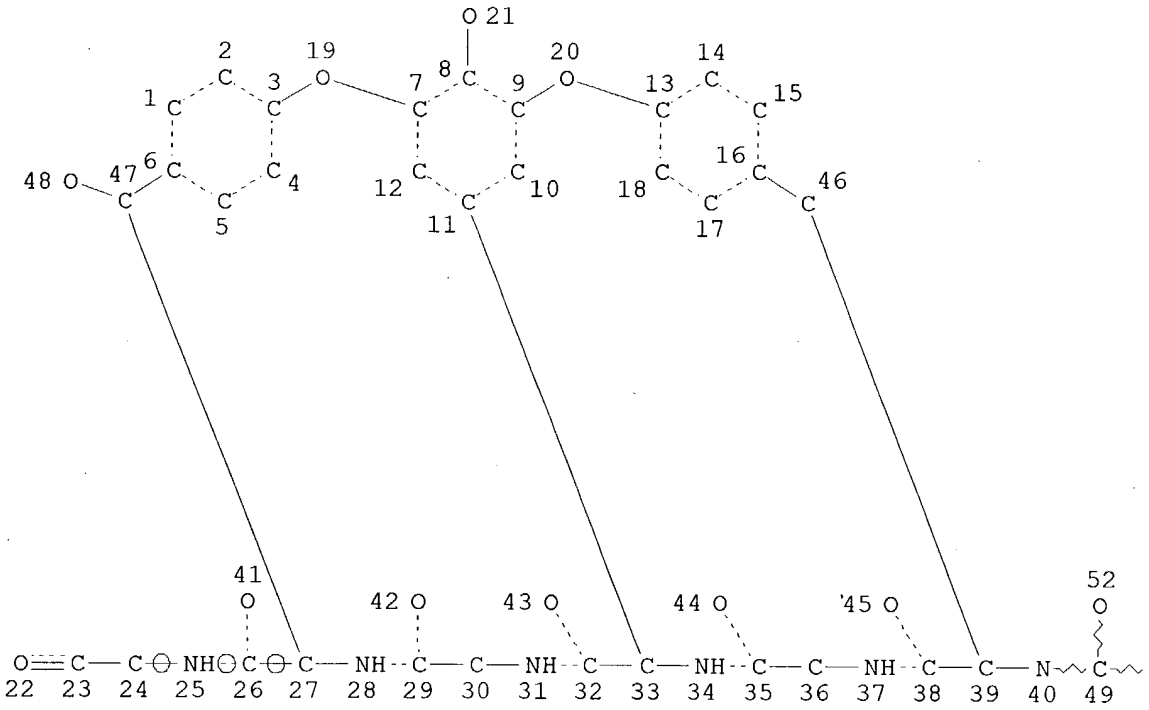
Searched by: Mary Hale 308-4258 CM-1 1E01



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Page 1-B
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 52

STEREO ATTRIBUTES: NONE
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100.0% PROCESSED 2856 ITERATIONS
SEARCH TIME: 00.00.01

2812 ANSWERS

didn't display too many hits

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	413.65	413.86

FILE 'MEDLINE' ENTERED AT 13:06:16 ON 23 SEP 2003

FILE 'CAPLUS' ENTERED AT 13:06:16 ON 23 SEP 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Searched by: Mary Hale 308-4258 CM-1 1E01

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=> fil medl,caplus,biosis,embase,jicst,wpids
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     4.41       4.41

FILE 'MEDLINE' ENTERED AT 16:16:42 ON 23 SEP 2003

FILE 'CAPLUS' ENTERED AT 16:16:42 ON 23 SEP 2003
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FILE 'JICST-EPLUS' ENTERED AT 16:16:42 ON 23 SEP 2003
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FILE 'WPIDS' ENTERED AT 16:16:42 ON 23 SEP 2003
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=> s reduc? alkylat? process?
L1            1 FILE MEDLINE
L2           13 FILE CAPLUS
L3            0 FILE BIOSIS
L4            1 FILE EMBASE
L5            1 FILE JICST-EPLUS
L6           11 FILE WPIDS

TOTAL FOR ALL FILES
L7           27 REDUC? ALKYLAT? PROCESS?

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8           23 DUP REM L7 (4 DUPLICATES REMOVED)

=> d 1-23 cbib abs;s reduc? alkylat? and (glycopeptid? or saccharide amino or
aldehyde? or ketone)

L8   ANSWER 1 OF 23  WPIDS  COPYRIGHT 2003 THOMSON DERWENT on STN
AN   2003-532318 [50]   WPIDS
AB   US2003088119 A UPAB: 20030805
     NOVELTY - Production of neotame (A) comprises using hydrogenation
     catalysts which have been either:
          (1) modified by multiple reuse in reductive
     alkylation process;
          (2) prepared to match physical properties of modified catalyst in
     (1);
          (3) modified by addition of catalyst modifier; or
          (4) modified by co-precipitation with metal from group VIII-IIB.
          DETAILED DESCRIPTION - Production of neotame of formula (A) comprises
     using hydrogenation catalysts which have been either:
          (1) modified by multiple reuse in reductive
     alkylation process;
          (2) prepared to match physical properties of modified catalyst in
     (1);
          (3) modified by addition of catalyst modifier to catalyst or reaction
```

mixture in a **reductive alkylation process;**
or

(4) modified by co-precipitation with metal from group VIII-IIB.

INDEPENDENT CLAIMS are also included for improving the selectivity of a hydrogenation catalyst comprising modifying it by the addition of either 0.0001-5% by weight of carbon dioxide, quinoline, morpholines, piperizine, pyridine, triphenylphosphine, phosphorous acid, thiocyanates, cyanamide, ethylenediamine, amidines, thiourea, ethyl di-isopropylamine, zinc, lead, silver, copper, mercury, tin, vanadium, other metallic salts, sodium hydroxide, ferrous sulfate or other salts, cadmium sulfate, or other salts, or lithium trioxide; or 1:1-1:0.05% by weight of a Group VIII-IIB metals.

USE - The method is used for producing neotame (claimed), an artificial sweetener.

ADVANTAGE - The invention uses modified catalysts, which improves the selectivity over conventional catalysts and reduces the level of certain impurities.

Dwg.0/0

L8 ANSWER 2 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-691594 [74] WPIDS
AB WO 200265853 A UPAB: 20021118

NOVELTY - Production of neotame comprises using hydrogenation catalyst (A) which:

(a) is modified by multiple reuse in a **reductive alkylation process;**

(b) is prepared to match the physical properties of modified catalyst (a);

(c) is modified by addition of a catalyst modifier to the catalyst or to the reaction mixture in a **reductive alkylation process,** or

(d) is modified by co-precipitation with Group VIII-IIB metal.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for coupling 3,3-dimethylbutyraldehyde (I) and aspartame (II) to produce neotame which comprises reductive alkylation of (I) and (II) in the presence of the hydrogen and at least one (A).

ACTIVITY - None given in the source material.

MECHANISM OF ACTION - None given in the source material.

USE - Used for the production of neotame used to impart sweetness to foods, beverages or other products.

ADVANTAGE - (A) Produces higher purity and yield of neotame with reduced cost. (A) Also reduces the level of dialkylated aspartame, one of the impurities resulting from conventional processes for manufacturing neotame.

Dwg.0/0

L8 ANSWER 3 OF 23 MEDLINE on STN DUPLICATE 1
2002374813 Document Number: 22116513. PubMed ID: 12120388. Diels-Alder chemistry of 2-diethoxyphosphinylcyclohex-2-enones. A new approach to complex phosphonates and synthetic applications of the beta-keto phosphonate system. Chien Chiung-Fang; Wu Jen-Dar; Ly Tai Wei; Shia Kak-Shan; Liu Hsing-Jang. (Department of Chemistry, National Tsing Hua University, Hsinchu, Taiwan 30013, Republic of China.) Chem Commun (Camb), (2002 Feb 7) (3) 248-9. Journal code: 9610838. ISSN: 1359-7345. Pub. country: England: United Kingdom. Language: English.
AB Enone phosphonates 1 and 2 were found to be excellent dienophiles for the Diels-Alder reaction, giving phosphonate-containing polycycles, and the phosphonate group of the resulting adducts facilitated both the installation of an angular alkyl group via a **reductive alkylation process** and the regioselective generation of

a ring junction double bond via an intramolecular Wadsworth-Horner-Emmons reaction.

L8 ANSWER 4 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2002-132169 [18] WPIDS
AB EP 1151995 A UPAB: 20020319
NOVELTY - Preparation of a polychelant involves reductive alkylation of a polyamino compound with a chelant compound in the presence of a reducing agent.

DETAILED DESCRIPTION - Preparation of a compound of formula L(NH2)p(NHF)z(N(F)2)x (I) involves reductive alkylation of the primary amino group of a compound of formula L(NH2)m (II) with an aldehyde of formula K-T-(CH2)q-1CHO (III) (3-40, preferably 10-35 fold molar excess) in the presence of a reducing agent (3-60 fold molar excess), in a reaction medium at -5 to 60 (preferably 15-30) deg. C. The reducing agent is sodium cyanoborohydride, pyridine borane, or trimethylamine borane. The reaction medium is aqueous buffer with a pH of 5-10, low molecular weight alcohol, and/or aprotic dipolar solvent.

L = organic backbone carrying primary amino groups;
m = 1 - 1000;
p and z = 0 - 999;
x = 1 - 1000;
p+z+x = m;
F = -(CH2)q-T-K;
q = 1 - 10;
T = a simple bond or an aliphatic chain, interrupted or not by O, N, S or by functional groups selected from (thio)carbonyl, amide, ester, thiourea or thioamide or aromatic residues (in which the chain is linked covalently to C, O, N or P atom of a residue K);
K = residue of a linear or cyclic polyaminopolycarboxylic, polyaminopolyphosphonic, polyaminopolyphosphoric or polyaminopolyphosphinic chelant, or one of their chelates with bi- or tri-valent ions of paramagnetic metals or radioisotopes, or their salts.

The chelated ions are selected from the bi- or trivalent ions i).

USE - (I) are useful for diagnostic imaging as general or specific contrast agent for specific tissues, organs or body compartments. Can be used in nuclear medicine and can also be encapsulated in liposomes, employed as single or multilamellar residues.

ADVANTAGE - The **reductive alkylation process** yields a number of diagnostically or therapeutically active sites per molecule that is greater than that obtainable from the current methods. It is possible to obtain lysine derivatives at least with two chelant/chelate residues on one of the two groups, or even, two chelant/chelate residues for each one of the primary amino groups with the advantage that the quantity of dermatan sulfate necessary to obtain the same diagnostic effect is at least halved, as are, in consequence, also its anticoagulant effect, and the resulting ion pair is stabilized by the high positive charge of the lysine derivative, since in this case amino groups are not acylated as in WO95/14491, but alkylated. Tertiary amines can be obtained in good yield even when large aldehydes are taken as the starting material and the primary amino groups belongs even to macromolecules. By using the process it is convenient to conjugate directly and with high yield the amino or polyamino carriers with metal complexes of the chelants, and the products obtained do not require a subsequent complexation step, so that an incomplete and/or non-specific incorporation of the metal ions into the complex is avoided. The purification of the final product is much more straight forward to perform.
Dwg.0/0

L8 ANSWER 5 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
2001:775195 Document No. 136:53433 x-ray photoelectron spectroscopy and x-ray diffraction studies on deactivation of barium promoted copper chromium oxide catalyst used in the synthesis of N-isopropylaniline. Pillai, R. B. C. (Department of Chemistry, Indian Institute of Technology, Madras, 600 036, India). Oriental Journal of Chemistry, 17(2), 187-190 (English) 2001. CODEN: OJCHEG. ISSN: 0970-020X. Publisher: Oriental Scientific Publishing Co..

AB N-Isopropylaniline was synthesized by reductive alkylation of aniline with acetone in the presence of H and Cu chromite at 140.degree. and 50 Kg/cm2 pressure. The rapid deactivation of the catalyst is the major problem encountered in this process. The surface of the catalyst was poisoned by nitrogenous org. compds. and the active species of the catalyst (Cu+) got reduced to Cuo state during the reaction under the influence of H at high pressure are the major causes for the deactivation. A study on the activity and deactivation of Ba promoted Cu chromite in **reductive alkylation process** is reported.

L8 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1999:53407 Document No. 130:96858 **Reductive alkylation process** to prepare tertiary aminoaryl cyan dye-transfer intermediates. Mylroie, Victor L. (Eastman Kodak Company, USA). U.S. US 5861535 A 19990119, 7 pp. (English). CODEN: USXXAM. APPLICATION: US 1997-935684 19970923.

AB Tertiary-aminoaryl compds. [e.g., N,N-(dialkylamino)aryl compds.], useful as cyan dye-transfer intermediates (no data), are prepd. using successive reductive steps without intermediate isolation by reducing a nitroaryl compd. in the presence of a ketone as both solvent and reactant and a hydrogenation catalyst under elevated hydrogen pressure and temp. and the intermediate is further reacted with an aldehyde in the same reaction mixt. without isolation to provide the second substituent on the amino group. Thus, 4-nitroacetanilide was reductively alkylated with acetone at 100.degree./1000 psig of hydrogen in the presence of a Pt/C catalyst, followed by a second reductive alkylation at 100.degree./800 psig of hydrogen with acetaldehyde, producing 4-(N-ethyl-N-isopropylamino)acetanilide in 99.2-99.5% yield.

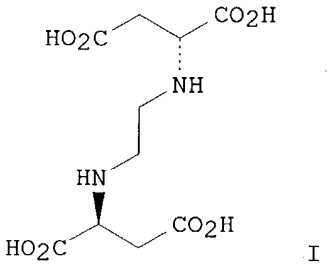
L8 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1998:530513 The development and optimization of pyridine.sum.borane complex as a reducing agent for the reductive alkylation of glycopeptide nucleus 264826.. Zheng, H.; Berglund, R. A. (Tippecanoe Laboratories, Eli Lilly and Company, Lafayette, IN, 47903, USA). Book of Abstracts, 216th ACS National Meeting, Boston, August 23-27, ORGN-150. American Chemical Society: Washington, D. C. (English) 1998. CODEN: 66KYA2.

AB In order to avoid using highly toxic sodium cyanoborohydride in the reductive alkylation of glycopeptide nucleus 264826, a series of amine.sum.borane complexes were screened. Among these complexes, pyridine.sum.borane was found to perform extremely well in the reaction. In combination with cupric acetate, and through the use of a portionwise addn. protocol for the reductant, yields similar to those obtained with the combination of cyanoborohydride and copper were obsd. These yields were about 20% higher than those obtained in the original **reductive alkylation process** and regioselectivity also improved significantly. Thus, pyridine.sum.borane was established as a viable alternative for sodium cyanoborohydride in the reductive alkylation of glycopeptide.

L8 ANSWER 8 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2
1996:743583 Document No. 126:19335 **Reductive alkylation process** for the preparation of compounds containing at least two

amino groups. Cowton, Elizabeth Lucy Mary; Bassett, Derek Anthony (The Associated Octel Company Limited, UK). PCT Int. Appl. WO 9632371 A1 19961017, 20 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-GB894 19960412. PRIORITY: GB 1995-7659 19950413.

GI



I

AB An alkylation process is described. The process comprises reacting at least a first nitrogen compd. and a second nitrogen compd. with a carbonyl compd. in the presence of a reducing agent to form a product comprising at least two nitrogen groups; wherein the carbonyl compd. comprises at least two carbonyl groups, the first nitrogen compd. comprises a first nitrogen group reactive with one carbonyl group of the carbonyl compd. and the second nitrogen compd. comprises a second nitrogen group reactive with the other (or another) carbonyl group of the carbonyl compd., and wherein at least the first nitrogen compd. or at least the second nitrogen compd. comprises at least one other functional group. The process is esp. suitable for the prepn. of (S,S)-ethylenediaminedisuccinic acid (EDDS) (I). Thus, treatment of 5.39 g L-aspartic acid and 5.89 g glyoxal in 50 mL water adjusted to pH 13.53 with 50% aq. NaOH with 1.74 g NaBH4 added portionwise over 2 h gave 52% isolated I after acidification with HCl to pH 2.6.

L8 ANSWER 9 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1995-372544 [48] WPIDS
AB RD 376051 A UPAB: 19951204
N-(4-((1-methylethyl)amino)phenyl) acetamide can be prepared by reacting N-(4-nitrophenyl)acetamide in the presence of 5% platinum on carbon catalyst (selectively poisoned, such as with sulphur) and acetone. The reaction solvent is ethanol. This process first reduces the nitro group on the starting material to an amine, which in the presence of acetone, reacts to form a Schiff base that is further reduced to give the final product. For the reaction, acetone is present in an amount of from about 4 to about 6 equivalents, with about 4.6 equivalents being preferred. Reaction temperature should be from about 90 to about 100deg.C with about 100deg.C being preferred. The reaction pressure is at least 800 psi hydrogen with a pressure of about 1000 psi hydrogen being preferred. Suitable variations of temperature and pressure would be readily apparent to a skilled artisan from this disclosure.

ADVANTAGE - The described conditions and reactants allow the reaction to be carried out within a few hours, typically less than 6 hours, and preferably within about 4-4.5 hours, using ethanol as an environmentally suitable solvent.

Searched by: Mary Hale 308-4258 CM-1 1E01

L8 ANSWER 10 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1996:143470 Document No. 124:201745 **Reduction alkylation process**. Anon. (UK). Research Disclosure, 376, P564, 37651 (English) 1995. CODEN: RSDSBB. ISSN: 0374-4353. Publisher: Kenneth Mason Publications Ltd..
AB N-{4-[(1-methylethyl)amino]phenyl}acetamide is prepd. by hydrogenation of N-(4-nitrophenyl)acetamide at 90-100.degree. (preferably 100.degree.) and >800 psi H2 (preferably .apprx.1000 psi H2) in the presence of acetone and selectively poisoned (e.g., with S) 5% Pt/C hydrogenation-reductive alkylation catalyst. The reaction is complete within <6 h (preferably 4-4.5 h).

L8 ANSWER 11 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1995:534195 Document No. 123:143602 Highly selective catalysts in reductive alkylations and in debenzylation in the presence of aromatic chlorine. Scaros, Mike G.; Yonan, Peter K.; Prunier, Michael L.; Laneman, Scott A.; Goodmonson, Owen J.; Friedman, Robert Mark (Department Chemical Sciences, G. D. Searle, Skokie, IL, USA). Chemical Industries (Dekker), 62(Catalysis of Organic Reactions), 457-60 (English) 1995. CODEN: CHEIDI. ISSN: 0737-8025. Publisher: Dekker.
AB Two highly selective hydrogenations based on sequential reductive alkylation and debenzylation were developed for the synthesis of bidisomide. The **reductive alkylation process** eliminates the use of carcinogenic ethylene oxide and impurities resulting from side reactions. The second hydrogenation step is the first reported debenzylation of a tertiary amine in the presence of an arom. chloride with selectivities of <0.5% dechlorination products obsd.

L8 ANSWER 12 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3
1995:367358 Document No. 122:143700 Hydrogenation catalysts and processes for specialty chemicals. Muroi, Takashiro (Chem. Catal. Dep., N. E. Chemcat Corp., Tokyo, 105, Japan). Shokubai, 37(1), 10-16 (Japanese) 1995. CODEN: SHKUAJ. ISSN: 0559-8958. Publisher: Shokubai Gakkai.
AB A review with 32 refs. The hydrogenation process is one of the most important steps in specialty chems. because the processes take many steps and the high cost of raw materials. Recent interesting hydrogenation processes and catalysts are introduced. Hydrogenation of nitro compds. is very familiar in the dye stuff industry. Hydrogenolysis is the most important process to make medicine, taking out acyl and benzyl compds. which were used as blocking agents. Hydrodechlorination and **reductive alkylation processes** are familiar in agricultural chem. and rubber industries. Hydrogenation of aroms. is necessary to produce specialty polymers.

L8 ANSWER 13 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1991-022927 [04] WPIDS
AB DE 3921447 A UPAB: 19930928
Prepn. of N-alkyl-haloanilines (I) comprises reacting a halonitrobenzene (II) with at least a stoichiometric amt. of a ketone R1-CO-R2 (III) in an inert organic solvent at 10-100 deg.C under 0-50 bar H2 pressure in the presence of a Pt/active C catalyst. In formulae, X = Cl or Br; n = 1 or 2; R1 = 1-4C alkyl and R2 = 1-6C alkyl or CR1R2 = 5- or 6-membered cycloalkane ring.

Halonitrobenzene is pref. o- or p-nitrochlorobenzene, p-bromonitrobenzene or 2,5-, 3,4-, 3,5-, 2,4- or 2,3-dichloronitrobenzene. Ketone is pref. acetone, diethyl ketone, methyl ethyl ketone, methyl isobutyl ketone, methyl isopropyl ketone, ethyl amyl ketone, ethyl isoamyl ketone, cyclopentanone or cyclohexanone. Solvent is pref. methanol, ethanol, isopropanol, isobutanol, ethyl acetate, n-butyl acetate,

isopropyl acetate, isoamyl alcohol or 2-ethylhexanol. Catalyst is pref. used in amts. of 2-10, esp. 3-5, wt.% based on cpd. (II). A sulphite-deactivated 5 wt.% Pt/active C catalyst is prefd.. The reaction is pref. carried out at 30-50 deg.C and at 5-25 bar H2 pressure.

USE/ADVANTAGE - Cpds. (I) are intermediate for pharmaceuticals, plant protectants and azo dyestuffs. The new process is economically and ecologically superior to the processes of DE 2941070 and US 3350450.
0/0

ABEQ US 5292957 A UPAB: 19940421

A new process for prepn. of N-alkylhalogenoanilines of formula (I) comprises reacting a halogenonitrobenzene of formula (II) with 1-1.5 times stoichiometric amt. of carbonyl cpd. of formula (III) in inert organic solvent at 30-50 deg.C, H2 superatmos. pressure of 0-50(5-25) bar in presence of 2-10(3-5) % wt. w.r.t. (II) of sulphited Pt/on activated C catalyst. In the formula, X is Cl or Br; n is 1 or 2; R1 is 1-4C alkyl; R2 is 1-6C alkyl; or R1 and R2 together with attached C form 5 or 6-membered cycloalkane.

USE/ADVANTAGE - Intermediates to plant protection agents, pharmaceuticals and dyes. An ecologically and economically improved **reductive alkylation process.**
Dwg.0/0

ABEQ EP 479877 B UPAB: 19941122

A process for the preparation of N-alkylhaloanilines of the formula (I) in which X is a chlorine or bromine atom and n is the number 1 or 2, R1 is a linear or branched alkyl (C1-C4) radical, R2 a linear or branched alkyl (C1-C6) radical or R1 and R2 together with the carbon atom to which they are bound can form a five- or six-membered cycloalkane ring, which comprises reacting a halonitrobenzene of the formula (II) in which X and n have the abovementioned meanings with from 1 to 1.5 times the stoichiometric amount of a carbonyl compound of the formula (III) in which R1 and R2 have the abovementioned meanings or R1 and R2 together with the carbon atom of the carbonyl group can form a five- or six-membered cycloalkane ring,in an organic solvent which is inert towards the reactants under the reaction conditions at temperatures of from 30 to 50 deg.C, at a hydrogen superatmospheric pressure of from 0 to 50 bar, in the presence of a sulphited platinum catalyst on activated carbon.
Dwg.0/0

L8 ANSWER 14 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN

1992:150961 Document No. 116:150961 Radical anions of aromatic compounds. XVIII. Reaction of products from one-electron potassium reduction of 9-cyanoanthracene with primary alkyl halides in liquid ammonia. Bil'kis, I. I.; Vaganova, T. A.; Pimnev, S. M.; Shteingarts, V. D. (Novosib. Inst. Org. Khim., Novosibirsk, USSR). Zhurnal Organicheskoi Khimii, 27(8), 1722-7 (Russian) 1991. CODEN: ZORKAE. ISSN: 0514-7492.

AB Redn. of 9-cyanoanthracene (I) with K in liq. NH3, followed by BuBr alkylation, afforded 80% 9-cyano-9-butyl-9,10-dihydroanthracene (II), corresponding to ipso alkylation of the intermediate anion radical. Formation of 9-cyano-9-(cyclopropylmethyl)-9,10-dihydroanthracene in reaction of I.bul.- with cyclopropylmethyl bromide indicated I.bul.- is alkylated in a classical nucleophilic substitution process. Addn. of H2O to the K+I.bul.- reaction mixt. followed by BuBr afforded anthrone dimer III with no II.

L8 ANSWER 15 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1990-024097 [04] WPIDS

AB EP 351684 A UPAB: 19930928

A **reductive alkylation process** is claimed for prepn. of N15,N15-dialkyl derivs. of teicophanin cpds. of formula (I) and addn. salts: where R1, R2 = 1-12C alkyl, 4-7C cycloalkyl,

cyano-(103C)alkyl, or phenyl-(1-4C)alkyl where the phenyl is opt. substd. in ortho, metal and/or para posn. with 1-3 of 1-4C alkyl, NO2, halogen, 1-4C alkoxy and phenyl; A = H or N-((9-12C)aliphatic acyl)-beta-D-2-deoxy -2-amino-glucopyranosyl; B = H or N-acetyl-beta-D-2-deoxy -2-amino-glucopyranosyl; M = H or alpha-D-mannopyranosyl; with the proviso that B = H only when A=M=H. The process is characterised in that: (a) to a suspension of a teicophanin cpd. (II), of formula (I) (where -NR1R2 is replaced by -NR3R4 (where R3 = H and R4 = H or value of R1, R2), in an organic polar protic solvent is added an at least 30 molar excess (w.r.t. (II)) of a carbonyl cpd. having the same C skeleton of R1, R3 and whose oxo gp. is on the C atom which is to bond to the N15-amino gp. of the teicophanin moiety, in the presence of an organic acid of such strength and in such amt. that dilution of the mixt. with 4 vols. of water gives a mixt. of pH 2.5-4, the acid being further characterised in that, under the reaction conditions it cannot yield a reduction prod. which is a competitor of the carbonyl cpd. in the reaction with the N15-amino gp.; and (b) the mixt. is reacted with an alkali metal borohydride at 0-60 deg. C.

USE/ADVANTAGE - (I) have antibacterial activity mainly against Gram positive bacteria. and are also useful as animal growth promoters. The process gives symmetrical or unsymmetrical dialkyl derivs. in good yields and with good selectivity, with fast conversion rates and low side-reactions and by-prods., and in a "one-pot" process. Complicated and expensive purification steps are not necessary. (I) may be admin. enterally, topically or pref. parenterally. Doses are 0.5-30 mg/kg, pref. divided in 2-4 doses/day.

0/0

L8 ANSWER 16 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 1984-188557 [30] WPIDS

CR 1983-782880 [40]

AB US 4459417 A UPAB: 19930925

Prepn. of spectinomycin analogues of formula (I) is from a corresp. cpd. of formula (II) by treatment with O2 in presence of a catalyst at 0-100 deg.C in aq. solvent. The prod. is protected with PhCH2O-CO or tBuO-CO, sepd. and deprotected to give a deriv. of formula (III). This prod. is alkylated with MeCHO in presence of NaCNBH3 at pH 3-6. R3= R4= Et; or R3= Me and R4= Et or R3= Et and R4= Me ((I) is a mixt. of these 2 cpds.); R,R'= H, 1-8C alkyl, 2-8C alkenyl, 1-8C haloalkyl, 1-8C aminoalkyl, 2-8C alkynyl, OX or (CH2)n-OX; n= 1-4; X= 1-4C alkyl, 2-8C alkenyl, benzyl or 1-5C alkanoyl; R1= R2= H; or R1= H and R2= Me or R1= Me and R2= H ((I) is a mixt. of these 2 cpds.).

Prepn. of N,N'-didemethyl-N,N' -diethylspectinomycin i.e. (I; R3= R4= Et; R= Me, R'= H).

USES/ADVANTAGES - New route to (I) without unwanted redn. of the highly electrophilic C-3' carbonyl, and the reaction conditions for alkylation give only S-amine prods. and N,N-dialkylation is avoided. (I) and derivs. obtd. from them are antibacterials, see US 4405797 (83-782880/40).

0/0

L8 ANSWER 17 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN

1984:590866 Document No. 101:190866 The alkali metal reduction of pyrene - structural and preparative aspects. Schnieders, C.; Muellen, K.; Huber, W. (Inst. Org. Chem., Univ. Koeln, Cologne, D-5000/41, Fed. Rep. Ger.). Tetrahedron, 40(10), 1701-11 (English) 1984. CODEN: TETRAB. ISSN: 0040-4020.

AB Redn. of pyrene with alkali metals yields the corresponding dianion salts. The solvent, counterion and temp. must be carefully selected since side reactions such as protonation (e.g. in liq. ammonia) or cleavage of the

ethereal solvent occur readily. Moreover, the spectroscopic characterization of the dianion is complicated by rapid electron transfer processes. There is no exptl. evidence for distorted dianion structures or for further redn. of pyrene toward a tetraanion. Knowledge of the ionic .pi.-structures is essential for an understanding of **reductive alkylation processes.**

L8 ANSWER 18 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1979-75402B [42] WPIDS
CR 1978-86241A [48]
AB CH 613450 A UPAB: 19930901
Prepn. of new tetrahydropyridine and piperidine derivs. of formula (I) and their acid addn. salts is claimed. In (I) R1 is a 1-12C aliphatic hydrocarbon radical; R2 is H or lower alkyl; R3 and R4 are H, lower alkyl, lower alkoxy, F, Cl, Br, benzloxy or OH, or R3 can also be CF3, lower 1-hydroxyalkyl, lower 1-alkenyl or a 5-8C 1-hydroxycycloalkyl, 1-cycloalkenyl or cycloalkyl gp. or R3+R4 can be (CH2)3, (CH2)4 or 1,3-butadienylene; R5 is H or 1-4C alkyl; X and Y are H or together form a bond; with the proviso that R1 cannot be Me when R2=R3=R4=R5=H). Prepn. comprises reductive alkylation of the corresp. cpds. where R1=H with a carbonyl cpd. of formula R'1=O (where R'1 is a geminal divalent radical corresp. to the monovalent radical R1).

Cpds. (I) are monoamine oxidase inhibitors and serotinin, noradrenaline and tetrabenzaine antagonists, and are thus useful as antidepressants.

L8 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1970:12313 Document No. 72:12313 Reactions of epoxides of 5-norbornene-2,3-dicarboximides. Concerted, reductive cleavage of the imide ring by lithium aluminum hydride. Gray, Allan P.; Heitmeier, Donald E. (Neisler Lab., Inc., Decatur, IL, USA). Journal of Organic Chemistry, 34(11), 3253-9 (English) 1969. CODEN: JOCEAH. ISSN: 0022-3263.
AB Both N-phenethyl-exo-5,6-epoxynorbornane-endo-2,3-dicarboximide (I) and its exo-dicarboximide isomer (II) are stable to vigorous acid treatment. The stability of these norbornene epoxide systems under acid conditions is interpreted in terms of the electron-withdrawing effect of the carbonyl groups inhibiting carbonium ion formation, coupled with steric hindrance of the norbornyl system to intermol., backside nucleophilic attack. The epoxide function of these systems is also stable to intermol. attack under basic conditions. Intramol. opening of the epoxide ring by appropriately situated nucleophiles can of course occur with facility, and AcOOH epoxidn. of endo-3-(N-phenethylcarbamoyl)-5-norbornene-endo-2-carboxylic acid (III) proceeds with accompanying attack on the formed (or forming) epoxide function and f ormation of diol derivs. LiAlH4 redn. of N-phenethyl-5-norbornene-endo-2,3-dicarboximide gives the expected 4,7-methanohexahydroisoindole (IV). Redn. of III also yields IV in a **reductive alkylation process.** LiAlH4 redn. of II affords 2-phenethyl-exo-5,6-epoxyexo-4,7-methanoo ctahydroisoindole (V) retaining the oxirane ring. On the other hand, treatment of I with LiAlH4 yields N-phenethyl-end o-3-hydroxymethyl-exo-5-hydroxy-endo-2,6-meth-animinonorbornane (VI), f ormation of which requires reductive cleavage of both the imide and oxiran e rings. VI must arise via a concerted, intramol. process with participation by the epoxide function. Analogs of VI with other N-substituents, and their mono- and diacyl derivs. were prepd. Treatment of V with a small excess of ethereal HCl in the cold gives the normal HCl salt, but when V is subjected to a larger excess of ethereal HCl in the cold, a chlorohydrin is produced via a typical norbornyl carbonium ion rearrangement. This underlines the effect of the electron-withdrawing power of the carbonyl groups in stabilizing the norbornene epoxide system.

Searched by: Mary Hale 308-4258 CM-1 1E01

L8 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1967:516758 Document No. 67:116758 Substituted 7- and (or) 9-amino-6-methylenetetracyclines. Bitha, Panayota; Hlavka, Joseph J.; Martell, Michael J., Jr. (American Cyanamid Co.). U.S. US 3341586 19670912, 4 pp. (English). CODEN: USXXAM. APPLICATION: US 19660506.
GI For diagram(s), see printed CA Issue.
AB cf. preceding abstr. The title compds. were prepd. by a **reductive alkylation process** comprising interaction of I with a carbonyl compd. Nitronium tetrafluoroborate (1.5 millimoles) was added to a suspension of 1 millimole 6-methylene-5.alpha. hydroxytetracycline-HCl (I.HCl) (R = R1 = H), the mixt. stirred 2 hrs. at room temp., and treated with Et2O to ppt. 7- and 9-nitro derivs. of I (R or R1 = NO2) sepd. by partition chromatog. 11a-Chloro-5.alpha.-hydroxytetracycline (II) (3 millimoles) was suspended in 60 ml. H2O, the suspension cooled to 0-5.degree. the pH adjusted to 7.5 with N NaOH soln., and stirred an addnl. 15 min. at 0-5.degree.. Sulfanilic acid monohydrate (3.3 millimoles) was added to a soln. of 3.3 millimoles. anhyd. Na2CO3 in 12 ml. H2O, the mixt. heated to soln., cooled to 0-5.degree., and diazotized with a soln. of 3.6 millimoles NaNO2 in 3 ml. H2O. The mixt. was poured into a mixt. of 3.3 g. ice, and 0.69 ml. concd. HCl to give the diazonium salt. The pH of II was adjusted to 7.5, and treated with the suspension of the diazonium salt, the mixt. stirred 45 min. in an ice bath, and the soln. acidified to pH 1.5. The ppt., 7-(p-HSO3C6H4N2) deriv. (III) of II, was centrifuged, washed, and dried. A soln. of 100 mg. III in 5 ml. HF was stirred 30 min. at 0-5.degree., the acid stripped with a stream of N, the residue taken up in 2 ml. Me2CO, and the product, 7-(p-sulfophenylazo)-11a-chloro-6-methylene-5.alpha.-hydroxytetracycline (IV) pptd. with Et2O. A soln. of 200 mg. IV in 20 ml. ethylene glycol monomethyl ether was reduced over Pd-C at room temp. to give 7-amino-6-methylene-5.alpha.-hydroxytetracycline, I (R = NH2, R1 = H). A soln. of 100 mg. of the 7- and 9-nitro-11a-chloro-5.alpha.-hydroxytetracycline in 5 ml. HF stirred 30 min. at 0-5.degree. gave the corresponding 7- and 9-nitro-6-methylene-11a-chloro-5.alpha.-hydroxytetracycline. A soln. of the mixt. (90 mg.) from the HF reaction in 20 ml. H2O, treated with a soln. of 400 mg. NaHSO3 in 5 ml. H2O, the pH adjusted to 6, the soln. stirred 30 min., filtered, and filtrate freeze-dried gave the 7- and 9-nitro-6-methylene-5.alpha.-hydroxytetracycline, I (R or R1 = NO2) (V) sepd. by chromatog. The 7- and 9-nitro mixt. on redn. over Pd-C gave the corresponding NH2 derivs. (VI). A soln. of VI (100 mg.) in 10 ml. ethylene glycol monomethyl ether, treated with 0.05 ml. concd. H2SO4 and 0.4 ml. 40% aq. soln. H2CO, was reduced over Pd-C to give the two NMe2 derivs. (VII). A soln. of 50 mg. II in a soln. of 10 mg. NaNO2 in 5 ml. HF stirred 45 min. at ice bath temp. gave the 7- and 9-nitroso derivs., and these on redn. over Pd-C gave the corresponding amino derivs., and the latter on treatment with 40% aq. H2CO as described gave the corresponding NMe2 derivs. These compds. are biol. active, and have a broad spectrum of antibacterial activity. A summary of the in vitro activity of VII as compared with that of VI against a variety of disease causing microorganisms is given.

L8 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2003 ACS on STN
1967:516757 Document No. 67:116757 Substituted 7- and(or) 9-amino-6-deoxytetracyclines. Bitha, Panayota; Hlavka, Joseph J.; Martell, Michael J., Jr. (American Cyanamid Co.). U.S. US 3341585 19670912, 4 pp. (English). CODEN: USXXAM. APPLICATION: US 19660506.
GI For diagram(s), see printed CA Issue.
AB The title compds. were prepd. by a **reductive alkylation process** comprising interaction of I with a carbonyl compd. N-Chlorosuccinimide (1.05 equivs.) was added to a soln. of .alpha.-6-deoxy-5.alpha.-hydroxytetracycline (I) (configuration of 6-Me is

.alpha.) free base in 45 ml. 1,2-dimethoxyethane distd. from NaH, the mixt. stirred 10 min. at room temp., and added to 500 ml. heptane to give the 11a-chloro deriv. (II). I (1 millimole) was suspended in 22 ml. H2O, the suspension cooled to 0-5.degree. in an ice bath, the pH adjusted to 7.5 with N NaOH soln., and stirred 15 min. at 0-5.degree.. Sulfanilic acid monohydrate (1.1 mollimoles) was added to a soln. of anhyd. Na2CO3 (0.55 millimole) in 4 ml. H2O, and the mixt. heated to dissolve the acid, cooled to 0-5.degree., then mixed with a soln. of 1.2 millimoles NaNO2 in 1 ml. H2O. The mixt. was poured into 1.1 g. cracked ice and acidified with 2.75 millimoles concd. HCl to give the diazonium salt. A suspension of the diazonium salt was added slowly to II (kept at pH 7.5) and the red soln. obtained stirred 1 hr. at 0-5.degree., the ice bath removed, the soln. acidified to pH 1.5 with concd. HCl, and the solid 11a-Cl-7-(p-HO3SC6H4N:N) deriv. (III) centrifuged, washed (H2O), and dried. III (0.3 millimole) in 20 ml. ethylene glycol monomethyl ether acidified with 1 ml. 2N H2SO4 was reduced over 100 mg. 10% Pd-C, the mixt. filtered, and the filtrate evapd. to dryness. This gave the corresponding NH2 deriv. (IV). The above procedure was repeated, the filtrate mixed with 1.6 ml. 40% H2CO, and the redn. over Pd-C continued for 1 hr., the mixt. filtered, and the filtrate concd. to .apprx.5 ml. and dild. with Et2O to give the NMe2 deriv. (V). A suspension of 1.82 millimoles p-O2NC6H4N2.BF4 (VI) in 23 ml. H2O cooled to 0-5.degree. was added to a suspension cooled to 0-5.degree. of 1.64 millimoles II in 40 ml. H2O (kept at pH 7.5). After all the VI was added, the pH of the mixt. was adjusted to 8.5, and the red soln. stirred 10 min. at 0-5.degree., then acidified to pH 1.8 with concd. HCl and the red-brown ppt. of the 7-(p-O2NC6H4N2) deriv. (VII) centrifuged and dried. A soln. of .beta.-6-deoxy isomer of I (1 millimole) and 1.1 millimoles KNO3 in 10 ml. liquid HF was stirred in an ice bath 1 hr., the solvent stripped off with a stream of N, the residue taken up in 5 ml. Me2CO, and the product pptd. with Et2O. This gave the 7- and (or) 9-NO2 deriv. (VIII). The crude VIII (200 mg.) in ethylene glycol monomethyl ether on redn. over Pd-C as above gave the 7- and (or) 9-amino deriv. (IX). The two isomers were sepd. by partition chromatog. The crude IX (150 mg.) in 10 ml. ethylene glycol monomethyl ether treated with 1.2 ml. 40% H2CO soln., 0.1 ml. concd. HCl, gave on redn. over Pd-C the 7- and (or) 9-NMe2 deriv. (X). In all cases in which the .alpha.-6-deoxy or the .beta.-6-deoxy was obtained the corresponding .beta.-and .alpha.-isomer was also prepd. These compds. are biol. active and have as broad a spectrum of antibacterial activity as the previously known tetracyclines. A summary of the in vitro activity of X as compared with that of IX against a variety of disease-causing microorganisms is given.

L8 ANSWER 22 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1973-37127U [26] WPIDS
AB US 3739026 A UPAB: 19930831

Reductive alkylation process for producing an N-alkyl-substd. amine by reacting p-aminodiphenyl-amine, pref. N-phenyl, N'-4-methyl-2- pentyl-para-phenylenediamine, with a ketone, methyl isoamyl ketone and pref. methylisobutyl ketone, in the presence of hydrogen, with a catalytic amt. of (a) a nickel catalyst; (b) Si-contng. material e.g. mercaptobenzothiazole, pref. thiodipropionic acid so that (b) contains 0.10-4.0 g. S/100 g. Ni and (c) 0.005-0.100 g. molecular wt. toluene-sulphonic acid/100 gm. N.

L8 ANSWER 23 OF 23 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1968-89001P [00] WPIDS
AB GB 1064958 A UPAB: 19930831

Reductive alkylation process in which an amine or nitro compound

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is hydrogenerated in the presence of hydrogen and an aliphatic or aromatic aldehyde or an aliphatic or alkyl aryl ketone to give a corresponding amine, the hydrogenation catalyst being a platinum metal sulphide, esp. Pt or Rh.

Side reactions are avoided and the catalysts are insensitive to poisons, esp. S-contng.-compds., thus obviating the need for purified hydrogen.

(I) is an antiozonant for rubber, and (II) as a class are stabilisers and anti-cracking agents, as demonstrated in examples.

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L9           68 FILE MEDLINE
L10         852 FILE CAPLUS
L11         105 FILE BIOSIS
L12          85 FILE EMBASE
L13          22 FILE JICST-EPLUS
L14         200 FILE WPIDS

TOTAL FOR ALL FILES
L15        1332 REDUC? ALKYLAT? AND (GLYCOPEPTID? OR SACCHARIDE AMINO OR ALDEHYD
                E? OR KETONE)

=> s reduc? alkylat? and glycopeptid? and (saccharide amino or aldehyde? or ketone)
L16          1 FILE MEDLINE
L17          7 FILE CAPLUS
L18          1 FILE BIOSIS
L19          1 FILE EMBASE
L20          1 FILE JICST-EPLUS
L21          6 FILE WPIDS

TOTAL FOR ALL FILES
L22         17 REDUC? ALKYLAT? AND GLYCOPEPTID? AND (SACCHARIDE AMINO OR ALDEHY
               DE? OR KETONE)

=> s l22 nt l7
MISSING OPERATOR L22 NT
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l22 not l7
L23          1 FILE MEDLINE
L24          7 FILE CAPLUS
L25          1 FILE BIOSIS
L26          1 FILE EMBASE
L27          1 FILE JICST-EPLUS
L28          6 FILE WPIDS

TOTAL FOR ALL FILES
L29         17 L22 NOT L7

=> dup rem l29
PROCESSING COMPLETED FOR L29
L30          13 DUP REM L29 (4 DUPLICATES REMOVED)

=> d 1-13 cbib abs

L30  ANSWER 1 OF 13  WPIDS  COPYRIGHT 2003 THOMSON DERWENT on STN
AN   2003-479442 [45]   WPIDS
AB   US2003008812 A UPAB: 20030716


Searched by: Mary Hale 308-4258 CM-1 1E01
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NOVELTY - **Glycopeptide** antibiotic derivatives (I) and (II) are new.

DETAILED DESCRIPTION - **Glycopeptide** antibiotic derivatives of formula (I) or (II), their salts, stereoisomers and prodrugs are new.

R2 = H or saccharide (optionally substituted by Ra-YRb-(Z)x);

R3 = ORc, N(Rc)2, ORa-YRb-(Z)x, NRc-Ra-YRb-(Z)x, NRcRe or ORe;

R4 = R7 or saccharide (optionally substituted by Ra-YRb-(Z)x);

R7 = alkyl, alkenyl, alkynyl (all optionally substituted), H, Ra-YRb-(Z)x or C(O)Rd;

R5 = H, halo, CH(Rc)-N(Rc)2, CH(Rc)-NRcRe or CH(Rc)-NRc-Ra-YRb-(Z)x;

R6 = R7 or saccharide (optionally substituted by NRc-Ra-YRb-(Z)x); or

R5+R6 = heterocyclic ring optionally substituted by NRc-Ra-YRb-(Z)x;

R8-R11, R25 = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl (all optionally substituted), aryl, heteroaryl, heterocyclic or H; or

R8+R10 = Ar1OAr2;

Ar1, Ar2 = arylene or heteroarylene;

R12 = R11, C(O)Rd, C(=NH)Rd, CON(Rc)2, COORd, C(=NH)N(Rc)2 or Ra-YRb-(Z)x; or

NR11R12 = heterocyclic ring;

R13 = H or OR14;

R14 = H, C(O)Rd or saccharide;

R15 = H or Ra-YRb-(Z)x;

R16 = H or Me;

R17 = H or optionally substituted alkyl;

Ra = alkylene, alkenylene or alkynylene (all optionally substituted);

Rb = covalent bond or Ra;

Rc = R8 or C(O)Rd;

Rd = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl (all optionally substituted), aryl, heteroaryl or heterocyclic;

Re = saccharide group;

W = ORc, SRc, S-SRd, N(Rc)2, S(O)Rd, SO2Rd, NRc-C(O)Rd, OSO2Rd, OC(O)Rd, NRcSO2Rd, C(O)N(Rc)2, COORc, C(=NRc)ORc, SO2N(Rc)2, SO2ORc, P(O)(ORc)2, P(O)(ORc)N(Rc)2, OP(O)(ORc)2, OP(O)(ORc)N(Rc)2, OCOORd, NRcCOORd, NRcCON(Rc)2, OCON(Rc)2, NRcSO2N(Rc)2, N+(Rc)=C(Rc)2, N=P(Rd)3, N+(Rd)3, P+(Rd)3, C(S)ORd or C(S)SRd;

X1-X3 = H or Cl;

Y = O, S, S-S, NRc, SO, SO2, NRcCO, OSO2, OC(O), NRcSO2, CONRc, C(O)O, SO2NRc, SO2O, P(O)(ORc)O, P(O)(ORc)NRc, OP(O)(ORc)O, OP(O)(ORc)NRc, OC(O)O, NRcCOO, NRcCONRc, OC(O)NRc or NRcSO2NRc-;

Z = H, aryl, heteroaryl, cycloalkyl, cycloalkenyl or heterocyclic;

n = 0-2;

x = 1-2;

R22 = ORc, N(Rc)2, ORa-YRb-(Z)x or NRc-Ra-YRb-(Z)x;

R23 = H, halo, CH(Rc)-N(Rc)2, CH(Rc)-R'e or CH(Rc)-NRcRa-YRb-(Z)x;

R24, R26 = H or lower alkyl; or

CR10NR11, CR25NR26 = heterocyclic ring; and

R'e = aminosaccharide group;

provided that:

(i) when Z = H, Rb is not a covalent bond;

(ii) at least one of R2-R7, R12 and R15 = -Ra-YRb-(Z)x;

(iii) when Y = NRc, Rc = 1-4C alkyl, Z = H and Rb = alkylene, then Rb contains at least 5C atoms;

(iv) when Y = CONRc, Z = H and Rb = alkylene, then Rb contains at least 5C atoms;

(v) when Y = S, Z = H and Rb = alkylene, then Rb contains at least 7C atoms;

(vi) when Y = O, Z = H and Rb = alkylene, then Rb contains at least 11C atoms; and

(vii) at least one of R12, R15, R22 and R23 = -Ra-YRb-(Z)x.

An INDEPENDENT CLAIM is also included for compounds of formula (III)

and their salts.

PG = H or a protecting group.

ACTIVITY - Antibacterial.

Test details are described but no biological data is given.

MECHANISM OF ACTION - None given.

USE - For treating a bacterial disease in a mammal (claimed). Also useful in the manufacture of a formulation or medicament useful as antibacterial agents.

ADVANTAGE - The compounds have enhanced activity, improved selectivity and reduced mammalian toxicity compared to the corresponding underivatized glycopeptides. The compounds are effective against broad spectrum of bacteria, including vancomycin resistant strains of bacteria. Dwg.0/0

L30 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

2001:816701 Document No. 135:344739 **Reductive alkylation** at saccharide amine of **glycopeptide** antibiotics. Linsell, Martin S. (Advanced Medicine, Inc., USA). PCT Int. Appl. WO 2001083521 A2 20011108, 53 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14017 20010501. PRIORITY: US 2000-PV201178 20000502; US 2000-PV213148 20000622.

AB A method for alkylating a **glycopeptide** at the saccharide amine group comprises combining an **aldehyde** or **ketone**, a base, and the **glycopeptide** or its salt, acidifying the mixt., and addn. of a reducing agent. In an example, a suspension of S-decylmercaptoacetaldehyde and vancomycin hydrochloride in DMF was stirred vigorously at room temp. for 2 h and then treated with CF3CO2H (90 min) and sodium cyanoborohydride/MeOH. After three hours, the reaction mixt. was analyzed by reverse-phase HPLC using the UV absorption at 280 nm to det. the product distribution. The product mixt. contained 77% (vs. 50% without intermediate acidification) of the compd. resulting from alkylation at the amino saccharide group and small amts. of compds. resulting from alkylation at the N-methylleucine group or from bisalkylation.

L30 ANSWER 3 OF 13 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN

AN 2001-557564 [62] WPIDS

AB WO 200157071 A UPAB: 20011026

NOVELTY - **Glycopeptide** derivatives (I), and their salts, prodrugs and stereoisomers, are new.

DETAILED DESCRIPTION - **Glycopeptide** derivatives of formula (I), and their salts, prodrugs and stereoisomers, are new.

R2 = H or a saccharide optionally substituted by Ra-Y-Rb-(Z)x;

R3 = ORc, NRcRc, ORa-Y-Rb-(Z)x, NRcRa-Y-Rb-(Z)x, NRcRe or ORe;

R4 = H or alkyl, alkenyl or alkynyl (all optionally substituted), Ra-Y-Rb-(Z)x, C(O)Rd, or a saccharide optionally substituted by Ra-Y-Rb-(Z)x;

R5 = H, halo, CH(Rc)N(Rc)2, CH(Rc)NRcRe, or CH(Rc)-NRc-Ra-Y-Rb-(Z)x;

R6 = H or alkyl, alkenyl or alkynyl (all optionally substituted), Ra-Y-Rb-(Z)x, C(O)Rd, or a saccharide optionally substituted by NRcRa-Y-Rb-(Z)x; or

R5+R6 = heterocyclyl optionally substituted by NRc-Ra-Y-Rb-(Z)x;

R8-R11 = H, or alkyl, alkenyl, alkynyl, cycloalkyl or cycloalkenyl

(all optionally substituted), or aryl, heteroaryl or heterocyclyl; or
R8+R10 = Ar1-O-Ar2;
Ar1, Ar2 = arylene or heteroarylene; or
R10+R11 = heterocyclyl;
R12 = H, or alkyl, alkenyl, alkynyl, cycloalkyl or cycloalkenyl (all optionally substituted), or aryl, heteroaryl, heterocyclyl, C(O)Rd, C(NH)Rd, C(O)NRcRc, C(O)ORd, C(NH)NRcRc or Ra-Y-Rb-(Z)x; or
R11+R12 = heterocyclyl;
R13 = H or OR14;
R14 = H, C(O)Rd or a saccharide;
R15 = H or Ra-Y-Rb-(Z)x;
R16 = H or CH3;
R17 = H, or alkyl (optionally substituted);
Ra = a bond, or alkylene, alkenylene, or alkynylene (optionally substituted);
Rb = a covalent bond, or alkylene, alkenylene, or alkynylene (all optionally substituted), provided that Rb is not a covalent bond when Z is H;
Rc = a bond, or alkyl, alkenylene, alkynylene, cycloalkyl, or cycloalkenyl (all optionally substituted), or aryl, heteroayl, heterocyclyl or C(O)Rd;
Rd = a bond, or alkyl, alkenylene, alkynylene, cycloalkyl, or cycloalkenyl (all optionally substituted), or aryl, heteroayl, or heterocyclyl ;
Re = a saccharide;
W = ORc, SRc, S-S-Rd, NRcRc, S(O)Rd, SO2Rd, NRcC(O)Rd, OSO2Rd, OC(O)Rd, NRcSO2Rd, C(O)NRcRc, C(O)ORc, C(NRc)OCRc, SO2NRcRc, SO2ORc, P(O)(ORc)2, P(O)(ORc)NRcRc, OP(O)(ORc)2, OP(O)(ORc)NRcRc, OC(O)ORd, NRcC(O)ORd, NRcC(O)NRcRc, OC(O)NRcRc, NRcSO2NRcRc, N+(Rc)=C(Rc)2, N=P(Rd)3, N+(Rd)3, P+(Rd)3, C(S)ORd or C(S)SRd;
X1-X3 = H or Cl;
Y = O, S, S-S, NRc, S(O), SO2, NRcC(O), OSO2, OC(O), NRcSO2, C(O)NRc, C(O)O, SO2NRc, SO2O, P(O)(ORc)O, P(O)(ORc)NRc, OP(O)(ORc)O, OP(O)(ORc)NRc, OC(O)O, NRcC(O)O, NRcC(O)NRc, OC(O)NRc, or NRcSO2NRc;
Z = H, aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclyl;
n = 0-2; and
x = 1 or 2;
provided that:
(i) at least one of R15, R2-R7 or R12 comprises a substituent of formula Ra-Y-Rb(Z)x;
(ii) when Y is NRc, Rc is 1-4C alkyl, Z is H and Rb is alkylene then Rb has at least 5C;
(iii) when Y is C(O)NRc, Z is H, and Rb is alkylene, then Rb has at least 5C;
(iv) when Y is S, Z is H and Rb is alkylene then Rb has at least 7C; and
(v) when Y is O, Z is H ane Rb is alkylene, then Rb has at least 11C.
An INDEPENDENT CLAIM is also included for a composition containing (I), and optionally a cyclodextrin.
ACTIVITY - Antibacterial.
No specific biological data given.
MECHANISM OF ACTION - None given.
USE - (I) are used for the treatment of bacterial diseases (claimed), especially those caused by Staphylococci (methicillin sensitive and resistant), Streptococci (penicillin sensitive and resistant), Enterococci (vancomycin sensitive and resistant) and Clostridium difficile.
ADVANTAGE - (I) have enhanced activity, improved selectivity and reduced toxicity compared to the corresponding underivatized glycopeptide. (I) are effective against a broad spectrum of bacteria, including vancomycin resistant strains of bacteria.

Dwg.0/0

L30 ANSWER 4 OF 13 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 2000-465734 [40] WPIDS
AB WO 200039156 A UPAB: 20000823
NOVELTY - **Glycopeptides** (I), useful as antibacterial agents, comprise at least one substituent (i).

DETAILED DESCRIPTION - **Glycopeptides** (I) or their salts, useful as antibacterial agents, comprise at least one substituent of formula (i).

Ra = alkene, alkenylene, alkynylene (all optionally substituted);

Rb = alkene, alkenylene, alkynylene (all optionally substituted) or a bond; provided that Rb is not a bond when Z is H;

Y' = O, S, -S-S-, -NRc-, -S(O)-, -SO2-, -NRcC(O)-, -OC(O)-, -NRcSO2-, -OSO2-, -C(O)NRc-, -SO2O-, -P(O)(ORc)O-, -P(O)(ORc)NRc-, -OP(O)(ORc)O-, -OP(O)(ORc)NRc-, -OC(O)O-, -NRcC(O)O-, -NRcC(O)NRc-, -OC(O)NRc- or -NRcSO2NRc-;

Z = H, aryl, cycloalkyl, cycloalkenyl, heteroaryl or heterocyclyl;

Rc = H, alkyl (optionally substituted), alkenyl (optionally substituted), alkynyl (optionally substituted), cycloalkyl (optionally substituted), cycloalkenyl (optionally substituted), aryl, heteroaryl, heterocyclyl or -C(O)Rd;

Rd = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl (all optionally substituted), aryl, heteroaryl or heterocyclyl;

x = 1 or 2; and

provided that:

(1) when Y' is -NRc-, Rc is 1-4C alkyl, Z is H and Rb is alkenylene, then Rb contains at least 5C;

(2) when Y' is -C(O)NRc-, Z is H and Rb is alkenylene, then Rb contains at least 5C;

(3) when Y' is S, Z is H and Rb is alkenylene, then Rb contains at least 7C; and

(4) when Y' is O, Z is H and Rb is alkenylene, then Rb contains at least 11C.

ACTIVITY - Antibacterial; antibiotic. Details of tests are described but no results are given.

MECHANISM OF ACTION - None given.

USE - The compounds (I) are useful for treating infectious diseases, especially infections by Gram-positive bacteria, in animals. (I) are particularly useful for treating methicillin-resistant staphylococci, enterococci and vancomycin-resistant enterococci infections, e.g. staphylococcal endocarditis or staphylococcal septicemia.

ADVANTAGE - (I) have an enhanced activity, selectivity and reduced mammalian toxicity compared to unsubstituted **glycopeptides**.

Dwg.0/0

L30 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
1998:351772 Document No. 129:28221 **Reductive alkylation** of **glycopeptide** antibiotics. Berglund, Richard A.; Lockwood, Nancy A.; Magadanz, Howard E.; Zheng, Hua (Eli Lilly and Co., USA; Berglund, Richard A.; Lockwood, Nancy A.; Magadanz, Howard E.; Zheng, Hua). PCT Int. Appl. WO 9822121 A1 19980528, 39 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US21238 19971120. PRIORITY: US 1996-31596 19961121.
AB **Glycopeptide** antibiotics comprising an amine-contg. saccharide at N4 and one or more other amines were **reductively**

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alkylated by treating a sol. copper complex of the **glycopeptide** antibiotic with a **ketone** or **aldehyde** in the presence of sodium cyanoborohydride or pyridine.borane complex. Thus, a mixt. of antibiotic A82846B, 4'-chloro-4-biphenylcarboxaldehyde, cupric acetate monohydrate, and sodium cyanoborohydride was refluxed in MeOH for 23 h to afford the copper complex of N4-[4-(4-chlorophenyl)benzyl]A82846B.

L30 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
1998:344629 Document No. 129:28220 Reducing agent for **reductive alkylation** of **glycopeptide** antibiotics. Berglund, Richard A.; Zheng, Hua (Eli Lilly and Co., USA; Berglund, Richard A.; Zheng, Hua). PCT Int. Appl. WO 9821952 A1 19980528, 29 pp. DESIGNATED STATES: W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US21126 19971120. PRIORITY: US 1996-31595 19961121.
AB Pyridine-borane is used as reducing agent for the **reductive alkylation** of amine-contg. **glycopeptide** antibiotics with an **aldehyde** or **ketone**. Thus, a mixt. of antibiotic A82846B, 4'-chloro-4-biphenylcarboxaldehyde, and pyridine-borane complex was refluxed in MeOH for 6 h to afford 53.2% N4-[4-(4-chlorophenyl)benzyl]A82846B.

L30 ANSWER 7 OF 13 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1998-288706 [26] WPIDS
AB EP 845478 A UPAB: 19980701
Reductive alkylation of a **glycopeptide** antibiotic with an amine-containing saccharide at N4 and one or more other amines, comprises reacting a soluble copper complex of the **glycopeptide** antibiotic with a **ketone** or **aldehyde** in the presence of sodium cyanoborohydride or a pyridine-borane complex.
USE - The process is used for **reductively alkylating glycopeptide** antibiotics.
ADVANTAGE - **Reductive alkylation** of the complex favours regioselective alkylation and gives increased yields.
Dwg.0/0

L30 ANSWER 8 OF 13 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
AN 1998-288705 [26] WPIDS
AB EP 845477 A UPAB: 19980701
Reductive alkylation of amine-containing **glycopeptide** antibiotics, comprises reacting a **glycopeptide** antibiotic with an **aldehyde** or **ketone** in the presence of pyridine-borane as the reducing agent.
USE - The method is useful for **reductively alkylating** an amine-containing **glycopeptide** antibiotic.
ADVANTAGE - The portion-wise addition of the pyridine-borane produces increased yields.
Dwg.0/0

L30 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
1996:740269 Document No. 126:19338 Preparation of **glycopeptide** antibiotic derivatives. Cooper, Robin D. G.; Huff, Bret E.; Nicas, Thalia I.; Quatroche, John T.; Rodriguez, Michael J.; Snyder, Nancy J.; Staszak, Michael A.; Thompson, Richard C.; Wilkie, Stephen C.; Zweifel, Mark J.

Searched by: Mary Hale 308-4258 CM-1 1E01

(Lilly, Eli, and Co., USA). PCT Int. Appl. WO 9630401 A1 19961003, 68 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US3550 19960314. PRIORITY: US 1995-410155 19950324.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides **glycopeptide** antibiotic deriv. compds. [I; X = H, Cl; R = N-R7a-(un)substituted 4-epivancosaminyl; R2 = NMeR7b; R6 = N-R7-(un)substituted 4-epivancosaminyl; R7, R7a, R7b = H, C2-16 alkenyl, C2-12 alkynyl, C1-12 alkyl-R8, C1-12 haloalkyl, C2-6 alkenyl-R8, C2-6 alkynyl-R8, C1-12 alkoxy-R8; provided that R7 = R7a = R7b .noteq. H; R8 = (un)substituted multicyclic aryl, heteroaryl, Ph, or C4-10 cycloalkyl, etc.]. These deriv. compds. possess antibacterial activity against a wide variety of bacteria, including activity against vancomycin-resistant isolates. In general, I were prepd. by **reductive alkylation** of the **glycopeptide** A82846B, i.e. I (R = R1 = 4-epivancosaminyl, R2 = R6 = H, R4 = CH2CHMe2, CH2CONH2, X = Y = Cl), with **aldehydes**. I [R = R1 = N-(4-nitrobenzyl)-4-epivancosaminyl, R2 = R6 = H, R4 = CH2CHMe2, CH2CONH2, X = Y = Cl] showed min. inhibitory concn. of .ltoreq.0.06, .ltoreq.0.06, .ltoreq.0.06, and 0.5 .mu.g/mL against Staphylococcus aureus 446, Enterococcus faecalis 276, E. gallinarum 245, and Escherichia coli EC14, resp. Tablets contg. 200 mg I.HCl [R = 4-epivancosaminyl, R1 = N-[4-(4-chlorophenyl)benzyl]-4-epivancosaminyl, R2 = R6 = H, R4 = CH2CHMe2, CH2CONH2, X = Y = Cl] were formulated.

L30 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
1996:390304 Document No. 125:143285 **Reductive alkylation** of **glycopeptide** antibiotics: synthesis and antibacterial activity. Cooper, Robin D. G.; Snyder, Nancy J.; Zweifel, , Mark J.; Staszak, Michael A.; Wilkie, Stephen C.; Nicas, Thalia I.; Mullen, Deborah L.; Futler, Thomas F.; Rodriguez, Michael J.; et al. (Infctious Diseases Res., Eli Lilly Co., Indianaplis, IN, 46285, USA). Journal of Antibiotics, 49(6), 575-581 (English) 1996. CODEN: JANTAJ. ISSN: 0021-8820. Publisher: Japan Antibiotics Research Association.

AB **Reductive alkylation** of the A82846 family of **glycopeptide** antibiotics has the potential of producing seven products. N-alkylation of the disaccharide amino group of these vancomycin derivs. can be accomplished selectively by treating a methanolic soln. of the **glycopeptide** with a slight excess of the desired **aldehyde**, heating to reflux and adding to the resulting soln. a suitable reducing agent such as NaBH3CN. Selective alkylation of the disaccharide amino group produces in products a large increase in antibacterial activity. For example, two products, LY 307599 and LY 333328, resulting from the N-alkylation of A82846B provide the most potent derivs. (i.e., 500 times) as compared to vancomycin, itself, against vancomycin-resistant enterococci.

L30 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2003 ACS on STN
1995:863062 Document No. 124:87732 **Reductive alkylation** of the **glycopeptide** antibiotic eremomycin and its derivatives. Pavlov, A. Yu.; Berdnikova, T. F.; Olsuf'eva, E. N.; Orlova, G. I.;

Preobrazhenskaya, M. N. (NII Izyskaniyu Nov. Antibiol., Moscow, Russia). Khimiko-Farmatsevticheskii Zhurnal, 29(1), 46-8 (Russian) 1995. CODEN: KHFZAN. ISSN: 0023-1134. Publisher: Meditsina.

AB Reaction of eremomycin and its derivs. with formaldehyde or benzaldehyde, followed by redn. with NaBH3CN yielded a series of Me and benzyl derivs. substituted at the amino groups. Some of the benzyl derivs. exhibited high antibacterial activity, but others showed lower activity than the parent antibiotic.

L30 ANSWER 12 OF 13 MEDLINE on STN DUPLICATE 2

89247371 Document Number: 89247371. PubMed ID: 2470404. Efficient coupling of **glycopeptides** to proteins with a heterobifunctional reagent. Lee R T; Wong T C; Lee R; Yue L; Lee Y C. (Department of Biology, Johns Hopkins University, Baltimore, Maryland 21218.) BIOCHEMISTRY, (1989 Feb 21) 28 (4) 1856-61. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB A heterobifunctional linking reagent containing a masked aldehydo group and acyl hydrazide was synthesized for coupling of **glycopeptides** and other amino-containing compounds to proteins. After conversion to acyl azide, the reagent reacts with the amino group of a **glycopeptide**, and the modified **glycopeptide** is deacetalized with a weak acid to unmask the aldehydo group, which is then conjugated to bovine serum albumin (BSA) by **reductive alkylation** with pyridine-borane. The overall reaction scheme proceeds under relatively mild conditions. When the protein amino group was in a large excess (greater than 6-fold) of the **aldehyde** reagent, the efficiency of conjugation was as high as 88% even at submicromole levels. As a test case for application of this reagent, 6-aminohexyl beta-D-galactopyranoside (Gal-AH) was attached to the linking reagent and conjugated to BSA at various **aldehyde**-to-protein molar ratios ranging from 25 to 200. The level of O-galactosyl residue incorporated into BSA by this reagent far exceeded that observed in a similar **reductive alkylation** involving S-galactoside reagents [Lee, R. T., & Lee, Y. C. (1980) Biochemistry 19, 156-163]. By use of the present conjugating procedure, as many as 112 mol of Gal-AH residues were incorporated per mole of BSA, which represents near total modification of the amino groups. Some binding characteristics of the new BSA derivatives were studied in the mammalian hepatic galactose/N-acetylgalactosamine specific lectin system along with other types of BSA derivatives (containing S-galactosyl residues). In general, the behavior of the new derivatives was similar to that of other types. For instance, the affinity increased exponentially at low sugar substitution levels (up to 30 mol of galactosyl residues/mol of BSA), and the slope of exponential increase and affinity at a given sugar substitution level was similar to those of other types.

L30 ANSWER 13 OF 13 JICST-EPlus COPYRIGHT 2003 JST on STN

890393650 Synthesis and antibacterial evaluation of N-alkyl vancomycins.. NAGARAJAN R; SCHABEL A A; OCCOLOWITZ J L; COUNTER F T; OTT J L; FELTY-DUCKWORTH A M. Lilly Research Lab., IN, USA. J Antibiot. (1989) vol. 42, no. 1, pp. 63-72. Journal Code: G0489A (Fig. 2, Tbl. 7, Ref. 9) CODEN: 0021-8820; Pub. Country: Japan. Language: English.

AB Over eighty N-alkyl vancomycins were synthesized by **reductive alkylation** of vancomycin with the appropriate **aldehydes**. The N-alkyl vancomycins exhibit greater antibacterial activity than the corresponding N-acyl vancomycins and the parent antibiotic. Some of these semisynthetic vancomycins are five times more active than vancomycin. The N-alkyl vancomycins also show longer elimination half-lives in rats than vancomycin.(author abst.)

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